REMARKS

I. Amendments

Claims 1-9 and 14-17 have been canceled. Claims 22-31 have been added. The newly added claims do not add or constitute new matter. Support for the newly added claims may be found throughout the specification and originally filed claims.

The foregoing amendments are made solely to expedite prosecution of the instant application, and are not intended to limit the scope of the invention. Further, the amendments to the claims are made without prejudice to the pending or now canceled claims or to any subject matter pursued in a related application. The Applicant reserves the right to prosecute any canceled subject matter at a later time or in a later filed divisional, continuation, or continuation-in-part application.

Upon entry of the amendment, 22-31 are pending in the instant application.

II. Rejections

A. Rejection under 35 U.S.C. § 112, first paragraph

The Examiner has rejected claims 3-9 and 14-17 under 35 U.S.C. 35 U.S.C. § 112, first paragraph, because the specification allegedly does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claim. Applicant respectfully traverses this rejection.

Specifically, the Examiner claims that while the specification is enabling for a homozygous knockout mouse comprising a disruption in the NTTP1 gene which results in no production of the NTTP1 protein, wherein said mouse exhibits the phenotype of anti-depressive behavior, a method of producing such a transgenic mouse by homologous recombination in mouse ES cells, and a cell isolated from said knockout mouse, it does not provide enablement for other transgenic and/or knockout animals comprising any disruption in the NTTP1 gene.

In view of the cancellation of claims 3-9 and 14-17, the Examiner's rejection of these claims under 35 U.S.C. 35 U.S.C. § 112, first paragraph are moot. Applicant, therefore, respectfully requests withdrawal of the rejection under 35 U.S.C. § 112, first paragraph. Applicant submits that new claims 22-31 fully meet the requirements and are patentable under 35 U.S.C. § 112, first paragraph.

B. Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 1, 2, 8, 14 and 15 under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention. Applicant respectfully traverses this rejection.

Regarding claims 1 and 2, the Examiner asserts that the term "selectable marker" renders the claims indefinite as it is unclear how a marker protein can be part of a vector construct. The Applicant disagrees, and believes the specification has clearly defined and described the term selectable marker and how it would be used in the targeting vector. However, as these claims have been canceled, and the newly added claims recite a selectable marker gene, this aspect of the rejection is no longer relevant.

The Examiner asserts that the arrangement of the target construct is unclear. Applicant submits that the new claims clearly set forth the relative arrangement of the elements of the targeting construct, rendering the Examiner's rejection moot.

Further, the Examiner asserts that the word "derived" renders claims 8 and 17 indefinite. Applicant respectfully disagrees. As can be found, for example, on page 2, lines 1-3 of the instant specification, the term "derived" is clearly defined and therefore not indefinite. Further, one of ordinary skill in the art would know to what the term "derived", in the context of cells and tissues "derived" from a transgenic mouse, relates. In any case, the current claims do not use the term "derived." Newly added claims use the term "obtained," which term is clear and definite. Therefore, the Examiner's rejection is no longer relevant.

Finally, the Examiner has alleged that the term "significant expression" renders claim 14 indefinite in that it is unclear what level of expression is considered to be significant. Although Applicant disagrees, and believes that one of skill in the art would know what level of expression would be considered significant, claim 14 has been canceled. New claims 22-31 no longer recite the term "significant expression."

Applicant submits that new claims 22-31 are definite and particularly point out and distinctly claim the subject matter regarded as the invention in accordance with 35 U.S.C. § 112, second paragraph.

C. Rejection under 35 U.S.C. § 103

Claims 1-9 stand rejected as being unpatentable under 35 U.S.C. § 103(a) based upon the teachings of Mansour *et al.*, 1988, *Nature* 336(24):348-352 ("Mansour"), in view of Theodosiou

et al., 1996, *Human Molecular Genetics* 5(5):675-684 ("Theodosiou"). Applicant respectfully traverses this rejection.

Mansour describes a general approach for isolating embryonic stem cells containing a targeted mutation in a gene, provided that a cloned fragment of the gene is available. Specifically, Mansour teaches the targeted disruption of the *hprt* gene and the proto-oncogene *int*-2 in mouse embryo-derived stem cells by homologous recombination using targeting constructs pRV9.1/TK and pINT-2-N/TK, respectively. The Examiner concedes, however, that Mansour does not teach how to make an NTTP1 receptor targeting construct and knockout mouse.

According to the Examiner, Theodosiou teaches the molecular cloning and characterization of NTTP1, a member of the MAP kinase phosphatase family, and describe the nucleic acid and amino acid sequence encoding NTTP1. Theodosiou also discloses that NTTP1 belongs to a dual-specificity tyrosine/threonine phosphatase family involved in MAP kinase signal transduction pathways.

As a basis of the obviousness rejection under 35 U.S.C. § 103, the Examiner asserts that the ordinary artisan would have been motivated to make a NTTP1 knockout construct and a transgenic knockout mouse in order to study the precise role that NTTP1 plays in cell signaling, as suggested by Theodosiou. The Examiner further asserts that the ordinary artisan would have had a reasonable expectation of success because of the teachings of Mansour and Theodosiou. The Applicant respectfully disagrees. However, in light of the cancellation of claims 1-9, the rejection is no longer relevant.

Claims 22-31 are drawn to a transgenic mouse comprising a homozygous disruption in an endogenous NTTP1 gene, which results in lack of production of functional NTTP1 protein, and leads to a phenotype of anti-depressive behavior, to a method of producing the mouse, to targeting constructs used to produce the mouse, and cells derived from the mouse, none of which are obvious in view of the sole or combined teachings of the cited references.

As the rejection under 35 U.S.C. § 103 is no longer relevant, and new claims 22-31 are not obvious in view of the sole or combined teachings of Mansour or Theodosiou, Applicant respectfully requests withdrawal of the rejection under 35 U.S.C. § 103.

It is believed that the claims are currently in condition for allowance, and notice to that effect is respectfully requested. The Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-1271 under Order No. R-690.

Respectfully submitted,

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